

? b 155

30aug02 13:29:12 User208669 Session D2097.1

\$0.37 0.105 DialUnits File1

\$0.37 Estimated cost File1

\$0.04 TELNET

\$0.41 Estimated cost this search

\$0.41 Estimated total session cost 0.105 DialUnits

File 155: MEDLINE(R) 1966-2002/Aug W4

\*File 155: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

# Set Items Description

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? s au=dong j?

S1 407 AU=DONG J?

? s aav and s1

998 AAV

407 S1

S2 5 AAV AND S1

? t s27/2

27/2

DIALOG(R)File 155: MEDLINE(R)

09949408 98374322 PMID: 9707617

Efficient expression of CFTR function with adeno-associated virus vectors that carry shortened CFTR genes.

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Adeno-associated virus (AAV)-based vectors have been shown to be effective in transferring the cystic fibrosis gene (CFTR) into airway epithelial cells in animal models and in patients. However, the level of CFTR gene expression has been low because the vector cannot accommodate the CFTR gene together with a promoter. In this study, we described a strategy to reduce the size of the CFTR cDNA to allow the incorporation of an effective promoter with the CFTR gene into AAV vectors. We engineered and tested 20 CFTR mini-genes containing deletions that were targeted to regions that may contain nonessential sequences. Functional analyses showed

that four of the shortened CFTRs (one with combined deletions) retained the function and the characteristics of a wild-type CFTR, as measured by open probability, time voltage dependence, and regulation by cAMP. By using an AAV vector with a P5 promoter, we transduced these short forms of CFTR genes into target cells and demonstrated high levels of CFTR expression. We also demonstrated that smaller AAV/CFTR vectors with a P5 promoter expressed the CFTR gene more efficiently than larger vectors or a vector in which CFTR gene was expressed from the AAV inverted terminal repeat sequence. The CFTR mini-gene with combined deletions was packaged into AAV virions more efficiently, generated higher titers of transducing virions, and more effectively transferred CFTR function into target cells. These new vectors should circumvent the limitations of AAV vector for CFTR expression. Our strategy also may be applicable to other genes, the sizes of which exceed the packaging limit of an AAV vector.

Record Date Created: 19980917

? log hold

30aug02 13:30:29 User208669 Session D2097.2

\$1.20 0.376 DialUnits File155

\$0.00 5 Type(s) in Format 6

\$0.21 1 Type(s) in Format 7

\$0.21 6 Types

\$1.41 Estimated cost File155

\$0.43 TELNET

\$1.84 Estimated cost this search

\$2.25 Estimated total session cost 0.481 DialUnits

Logoff: level 02.08.23 D 13:30:29

